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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/713,601	11/15/2000	Poonam Agarwal	FORS-04603	9798

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EXAMINER	
KIM, YOUNG J	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 12/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/713,601	AGARWAL ET AL.	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 November 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The Examiner of record has been changed. All further correspondence regarding this application should be directed to Examiner Young J. Kim whose Group Art Unit is 1637.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 23, 2003 has been entered.

Priority

Applicants are reminded that the first line of the specification contains an improper priority claim under 35 U.S.C. 120. Benefit claims under 35 U.S.C. 120 must include a specific reference to earlier filed (nonprovisional) applications for which a benefit is sought. A "specific reference" requires: (1) the identification of the prior (nonprovisional) application by **application number**; and (2) an indication of the **relationship** between the nonprovisional applications; except for the benefit claim to the prior application in a continued prosecution application (CPA).

For the instant application, the specification discloses that a priority claim is made to a listing of U.S. Patents (page 1, specification), thereby failing to meet the proper requirements for the benefit under 35 U.S.C. 120.

Since the corresponding Application Serial numbers are present in the Oath and Declaration, Applicants are advised to amend the specification appropriately.

Appropriate correction is required.

Information Disclosure Statement

The Office acknowledges the IDS received on September 26, 2003. The signed copy of its corresponding PTO-1449 is attached hereto.

Applicants are advised that the U.S. Applications which have not been published nor issued as patents are cited in the IDS. The U.S. Applications which have been published under pre-grant publication have been considered on PTO-1449. However, the U.S. Applications which have not been published nor patented, particularly, ref # 27, 30, and 33, have been considered for the record, but lined-through in the PTO-1449 as the inventive entity of the Applications are different from that of the instant Application.

Specification

The disclosure is objected to because of the following informalities: On page 29 of the specification, the specification refers to Figure 29 of the Drawing, referring to regions x and y. Figure 29 of the instant application, is a figure of gel electrophoresis. It appears that description is referring to Figure 25 of the instant application.

Appropriate correction is required.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 7-11 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 92 and 99-101 of copending Application No. 09/381,212 (IDS ref # 27). Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

Preliminarily, claims of the 09/381,212 application, hereto referred to as '212 application, has been allowed, but has not yet been issued as a patent. Therefore, the instant provisional rejection may be maintained under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the subsequently issued U. S. Patent.

Claims 7-11 of the instant application is drawn to a kit for detecting a target sequence comprising oligonucleotides capable of forming an invasive structure in the presence of said target sequence, wherein the kit further comprises an agent (claim 8) which is a cleavage agent (claim 9), and wherein the oligonucleotides of the kit are further described in claim 10. Claim 11 recites that the target sequence is derived from a list of sources selected from a Markush Group.

Claim 92 of the '212 application is drawn to a kit comprising a first and a second oligonucleotides, which are capable of forming an invasive structure as defined in the page 67-68

of the instant application (therefore meets the limitation of instant claim 7). Claim 92 also recites that the kit further comprises a structure-specific 5' nuclease, which meets the limitation of the "agent for detecting the presence of an invasive cleavage structure" of instant claim 8, as well as agent further defined as "a cleavage agent" in instant claim 9.

Claim 10 of the instant application is rendered obvious over claim 92 of the '212 application because both of the kits comprise the same description of the first and second oligonucleotides. Further, instant claim 10 depends from claim 7 which recites that the kit comprises an agent for detecting the presence of an invasive cleavage structure. The kit of claim 92 of the '212 application comprises a structure-specific 5' nuclease which is an agent for detecting such cleavage structure, as defined by lines 25-30 of page 69 of the instant application.

While claims 99-101 are not explicit in reciting the limitation of the instant claim 11, wherein the limitation requires the target sequence is selected from a Markush Group, consisting of human CMV DNA, polymorphisms in human apolipoprotein E gene, etc. (see instant claim 11), claim 99-101 requires the use of a thermostable structure-specific 5' nuclease, wherein several embodiments are drawn to a Flap-endonuclease, FEN-1 endonuclease, which would necessarily allow the detection of target sequences from the members of the claimed Markush Group.

For the above reasons, claims 7-11 of the instant application is rendered obvious over claims 92 and 99-101 of the '212 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-3 and 5 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 5, 6, and 7 of copending Application No. 10/290,386. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

The obviousness of the claims is illustrated claim by claim.

Claim 1 of the instant application is drawn to a method for detecting a target sequence via use of oligonucleotides capable of forming an *invasive cleavage structure* in the target sequence and an agent capable of cleaving said *invasive cleavage structure*, followed by a detection of the cleavage structure, effecting the detection of the target sequence.

Claim 1 of the 10/290,386 application, hereto referred to as '386 application, is drawn to a method for detecting target sequence via use of a sample containing synthetic DNA amplified from a genomic DNA, said genomic DNA harboring a target sequence, wherein the method is achieved by the use of oligonucleotides capable of forming an *invasive cleavage structure* with the synthetic DNA and an agent capable of cleaving said *invasive cleavage structure.*

Claim 1 of the instant application differs from claim 1 of '386 application in two ways: *i*) the instant claim recites a sub-step (c) which explicitly requires that the detection of cleavage structure is accomplished while claim 1 of '386 application is silent; and *ii*) the instant claim is broadly drawn to using a sample suspected of containing a target sequence while claim 1 of '386 application is requires a synthetic DNA produced from an amplification of a genomic.

With regard to the difference iterated in *i*), the explicit recitation that a detection is accomplished does not render the instant claim non-obvious over claim 1 of '386 application because the preambles of the both methods are clearly drawn to a *detection* method. Since, all of

the elements recited in both of the method claims require the same oligonucleotides as well as the *agent which detects the presence of an invasive cleavage structure*, one of ordinary skill in the would reasonably conclude that both of the method claims would *result in the detection of the target nucleic acid sequence*, and this regardless of whether an explicit statement as recited in sub-step (c) of the instant claim 1, is present or not. Even if, *arguendo*, that absence of such recitation is not obvious, claim 6 of '386 application explicitly recites that the method comprises a sub-step (c) which detects the cleavage of the invasive cleavage structure.

With regard to the difference iterated in *ii*), the amplification of the region of a genomic DNA sequence prior to the actual detection method, such as a polymerase chain reaction (PCR), is a well known technique in the art of nucleic acid detection. It is a well known in the art advantage that PCR allows the amplification of samples comprising target nucleic acid sequence, facilitating the detection of target nucleic acids as well as target nucleic acids which are minuscule in amount. Since the method of instant claim 1 *comprises* the recited sub-steps, such language would allow for, "*inclusion of unspecified ingredients even in major amount*," (*Ex parte Davis,* 80 USPQ 448, 450 (Bd. App. 1948)), allowing for "additional, unrecited elements or method steps" which would, "*still form a construct within the scope of the claim.*" (*Genentech, Inv. V. Chiron Corp.,* 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997))

Claim 2 of the instant application is verbatim to claim 2 of '386 application. Since both claims are dependent on claims 1 of the instant application and '386 application, the claims, for the reasons set forth above, claim 2 of the instant application is rendered obvious in view of claim 2 of '386 application.

Claim 3 of the instant application requires the same steps as claim 5 of '386 application. While instant claim 3 recites the detection from a target nucleic acid to the synthetic DNA of claim 5 of '386 application, the obviousness for the difference has already been discussed above. Since both claims are dependent on claims 2 of the instant application and '386 application, claim 3 of the instant application is rendered obvious in view of claim 5 of '386 application.

Claim 5 of the instant application different from claim 7 of '386 application in that instant claim 5 is drawn to the detection from a target nucleic acid while claim 7 of '386 application is drawn to the detection from a synthetic DNA target nucleic acid. The obviousness for such differences has been discussed above, rendering the instant claim 5 obvious over claim 7 of '386 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-3 and 5 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 16 of U.S. Patent No. 6,090,543 (IDS ref # 12). Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

Claim 1 of the instant application is drawn to a method for detecting a target sequence via use of oligonucleotides capable of forming an *invasive cleavage structure* in the target sequence and an agent capable of cleaving said *invasive cleavage structure*, followed by a detection of the cleavage structure, effecting the detection of the target sequence.

Claim 16 of U.S. Patent No. 6,090,543, hereto referred to as '543 patent, is drawn to a method for detecting a target nucleic acid molecule by detecting non-target cleavage products, via use of a first and second oligonucleotides, wherein the first and the second oligonucleotides form an invasive cleavage structure, as exemplified in Figure 25 of the instant application. Although claim 1 of the instant application requires an *agent* for detecting the presence of an invasive cleavage structure while claim 16 of '543 patent requires the use of *cleavage means,* the instant specification is clear that the agent must cleave the invasive cleavage structure (further evident from instant claim 2). Since claim 16 of '543 patent is clear that the cleavage means is employed for detection, instant claims 1 and 2 are obvious in view of claim 16 of '543 patent.

Claim 3 of the instant application recites that the method exposes the sample to the oligonucleotides to form an invasive cleavage structure and the invasive cleavage structure is cleaved by the cleaving agent.

Claim 16 of '543 patent recites that the method involves first and second oligonucleotides which produces a structure (sub-step (iii)) which is identical to the invasive cleavage structure depicted in Figure 25 of the instant application. Claim 16 also recites that the method introduces the cleavage means to generate a cleavage structure, meeting all of the limitations of instant claim 3.

Claim 5 of the instant application depends from the method of claim 1, wherein the target sequence comprises a first region and a second region, the first region which is upstream of the second region; a first oligonucleotide comprising a portion which is completely complementary to the first region of the target sequence; and a second oligonucleotide comprising a 5' portion which is completely complementary to the second region of the target sequence.

Claim 16 of '543 patent recites that the first oligonucleotide comprises a 3' portion which is complementary to a *third region* and the 5' portion of the first oligonucleotide and the 3' portion of the second oligonucleotide contains sequences which are full complementary to the *second region* of the target nucleotide. However, claim 16 defines that the *third* region is a region on the target nucleic acid which is located upstream of the *second* region. Based on this description, identical structure invasive cleavage structure would be produced, thereby meeting the limitations of claim 5.

While claims 1-3 and 5 of the instant application is rejected over claim 16 of the '543 patent, an obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would be obvious over, the reference claim(s). see, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Claims 1-3, and 5 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 5,846,717 (IDS ref # 17). Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

Claim 1 of the instant application is drawn to a method for detecting a target sequence via use of oligonucleotides capable of forming an *invasive cleavage structure* in the target sequence

and an agent capable of cleaving said *invasive cleavage structure*, followed by a detection of the cleavage structure, effecting the detection of the target sequence.

Claim 1 of U.S. Patent No. 5,846,717, hereto referred to as '717 patent, is drawn to a method for detecting a target nucleic acid molecule by detecting non-target cleavage products, via use of oligonucleotides capable of forming an *invasive cleavage structure*, as defined on page 69 of the instant specification, and a cleavage means, followed by the detection of the non-target cleavage product, which *is* the invasive cleavage structure, thereby meeting all of the limitation of instant claim 1.

Claim 2 of the instant application is drawn to an agent which is a cleavage agent. Claim 1 of '717 patent recites that the method involves a cleavage means which generates a cleavage product.

Claim 3 of the instant application and sub-step (b) of claim 1 of '717 patent, though not verbatim, achieves the same outcome. Both of the claims require the use of oligonucleotides, cleavage agent, and target nucleic acid to produce an invasive cleavage structure which is cleaved by the cleavage agent.

Claim 5 of the instant application recites the nature of the target nucleic acid and the nature of the oligonucleotides employed in the method.

Claim 1 of the '717 patent is different in that the first oligonucleotide comprises a 3' portion which is complementary to a *third region* and the 5' portion of the first oligonucleotide and the 3' portion of the second oligonucleotide contains sequences which are full complementary to the *second region* of the target nucleotide. However, claim 1 defines that the *third* region is a region on the target nucleic acid which is located upstream of the *second* region.

Based on this description, identical structure invasive cleavage structure would be produced, thereby meeting the limitations of claim 5.

While claims 1-3 and 5 of the instant application is rejected over claim 1 of the '717 patent, an obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would be obvious over, the reference claim(s). see, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Therefore, for the above reasons, claims 1-3 and 5 are rendered obvious in view of claim 1 of '717 patent.

Claims 1-3 and 5 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,348,314 (IDS ref # 9). Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

Claim 1 of the instant application is drawn to a method for detecting a target sequence via use of oligonucleotides capable of forming an *invasive cleavage structure* in the target sequence and an agent capable of cleaving said *invasive cleavage structure*, followed by a detection of the cleavage structure, effecting the detection of the target sequence.

Claim 1 of U.S. Patent No. 6,348,314, hereto referred to as '314 patent, is drawn to a method for detecting a target nucleic acid molecule by detecting non-target cleavage products,

via use of oligonucleotides capable of forming an *invasive cleavage structure*, as defined on page 69 of the instant specification, and a cleavage agent, followed by the detection of the non-target cleavage product, which *is* the invasive cleavage structure. Although claim 1 of '314 patent recites the nature of the target nucleic acid sequence as well as the mixture of the target nucleic acid with the oligonucleotides and the cleavage agent, such description is embraced by sub-step (b) of the instant claim 1, wherein it recites, "exposing the sample to said oligonucleotides and said agent," rendering instant claim 1 obvious in view of claim 1 of '314 patent.

Claim 2 of the instant application is drawn to an agent which is a cleavage agent. Claim 1 of '314 patent recites that the method involves a cleavage agent which generates a cleavage product.

Claim 3 of the instant application and sub-step (b) of claim 1 of '314 patent, though not verbatim, achieves the same outcome. Both of the claims require the use of oligonucleotides, cleavage agent, and target nucleic acid to produce an invasive cleavage structure which is cleaved by the cleavage agent.

Claim 5 of the instant application recites the nature of the target nucleic acid and the nature of the oligonucleotides employed in the method. Claim 1 of '314 patent, sub-step (a)(ii) and (iii) recites the same limitations.

While claims 1-3 and 5 of the instant application is rejected over claim 1 of the '314 patent, an obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would be obvious over, the reference claim(s). see, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir.

1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Therefore, for the above reasons, claims 1-3 and 5 are rendered obvious in view of claim 1 of '314 patent.

Claim 6 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 6 of copending Application No. 10/290,386 in view of Caskey et al (U.S. Patent No. 5,578,458, issued November 26, 1996).

Claim 6 of the instant application is drawn to a method for detecting a target sequence via use of oligonucleotides capable of forming an *invasive cleavage structure* in the target sequence and an agent capable of cleaving said *invasive cleavage structure*, followed by a detection of the cleavage structure, effecting the detection of the target sequence, wherein the target sequence is selected from a Markush Group.

Claim 1 of the 10/290,386 application, hereto referred to as '386 application, is drawn to a method for detecting target sequence via use of a sample containing synthetic DNA amplified from a genomic DNA, said genomic DNA harboring a target sequence, wherein the method is achieved by the use of oligonucleotides capable of forming an *invasive cleavage structure* with the synthetic DNA and an agent capable of cleaving said *invasive cleavage structure.*

Claim 6 of the instant application differs from claim 1 of '386 application in two ways: *i*) the instant claim recites a sub-step (c) which explicitly requires that the detection of cleavage structure is accomplished while claim 1 of '386 application is silent; and *ii*) the instant claim is

broadly drawn to using a sample suspected of containing a target sequence while claim 1 of '386 application is requires a synthetic DNA produced from an amplification of a genomic.

With regard to the difference iterated in *i*), the explicit recitation that a detection is accomplished does not render the instant claim non-obvious over claim 1 of '386 application because the preambles of the both methods is clearly drawn to a *detection* method. Since, all of the elements recited in both of the method claims require the same oligonucleotides as well as the *agent which detects the presence of an invasive cleavage structure*, one of ordinary skill in the would reasonably conclude that both of the method claims would *result in the detection of the target nucleic acid sequence*, and this regardless of whether an explicit statement as recited in sub-step (c) of the instant claim 6, is present or not. Even if, *arguendo*, that absence of such recitation is not obvious, claim 6 of '386 application explicitly recites that the method comprises a sub-step (c) which detects the cleavage of the invasive cleavage structure.

With regard to the difference iterated in *ii*), the amplification of the region of a genomic DNA sequence prior to the actual detection method, such as a polymerase chain reaction (PCR), is a well known technique in the art of nucleic acid detection. It is a well known in the art advantage that PCR allows the amplification of samples comprising target nucleic acid sequence, facilitating the detection of target nucleic acids as well as target nucleic acids which are minuscule in amount. Since the method of instant claim 6 *comprises* the recited sub-steps, such language would allow for, "*inclusion of unspecified ingredients even in major amount*," (*Ex parte Davis,* 80 USPQ 448, 450 (Bd. App. 1948)), allowing for "additional, unrecited elements or method steps" which would, "*still form a construct within the scope of the claim.*" (*Genentech, Inv. V. Chiron Corp.,* 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997))

While claim 1 of the '386 application does not explicitly state that the target nucleic acid sequence could be selected from a list of elements from the Markush group recited in instant claim 6, such limitation is considered to be obvious in view of the disclosure of Caskey et al., wherein the artisans explicitly state that, "various infectious disease can be diagnosed by the presence in clinical samples of specific DNA sequences characteristic of the causative microorganisms...includ[ing] viruses such as cytomegalovirus." (column 10, line 63 through column 11, line 13), cytomegalovirus being one of the elements recited in the Markush group of instant claim 6.

Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made, to become motivated to employ the detection method disclosed by the '386 application for the detection of cytomegalovirus, for the purpose of detecting whether a host was infected with such infectious microorganism, with a reasonable expectation of success.

This is a provisional obviousness-type double patenting rejection.

Claim 6 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 16 of U.S. Patent No. 6,090,543 (IDS ref # 12) in view of Caskey et al (U.S. Patent No. 5,578,458, issued November 26, 1996).

Claim 6 of the instant application is drawn to a method for detecting a target sequence via use of oligonucleotides capable of forming an *invasive cleavage structure* in the target sequence and an agent capable of cleaving said *invasive cleavage structure*, followed by a detection of the cleavage structure, effecting the detection of the target sequence, wherein the target sequence is selected from a Markush Group.

Claim 16 of U.S. Patent No. 6,090,543, hereto referred to as '543 patent, is drawn to a method for detecting a target nucleic acid molecule by detecting non-target cleavage products, via use of a first and second oligonucleotides, wherein the first and the second oligonucleotides form an invasive cleavage structure, as exemplified in Figure 25 of the instant application. Although claim 6 of the instant application requires an *agent* for detecting the presence of an invasive cleavage structure while claim 16 of '543 patent requires the use of *cleavage means,* the instant specification is clear that the agent must cleave the invasive cleavage structure (further evident from instant claim 2). Since claim 16 of '543 patent is clear that the cleavage means is employed for detection, instant claim 6 is obvious in view of claim 16 of '543 patent.

While claim 16 of the '543 patent does not explicitly state that the target nucleic acid sequence could be selected from a list of elements from the Markush group recited in instant claim 6, such limitation is considered to be obvious in view of the disclosure of Caskey et al., wherein the artisans explicitly state that, "various infectious disease can be diagnosed by the presence in clinical samples of specific DNA sequences characteristic of the causative microorganisms...includ[ing] viruses such as cytomegalovirus." (column 10, line 63 through column 11, line 13), cytomegalovirus being one of the elements recited in the Markush group of instant claim 6.

Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made, to become motivated to employ the detection method disclosed by the '543 patent for the detection of cytomegalovirus, for the purpose of detecting whether a host was infected with such infectious microorganism, with a reasonable expectation of success.

Claim 6 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 5,846,717 (IDS ref # 17) in view of Caskey et al (U.S. Patent No. 5,578,458, issued November 26, 1996).

Claim 6 of the instant application is drawn to a method for detecting a target sequence via use of oligonucleotides capable of forming an *invasive cleavage structure* in the target sequence and an agent capable of cleaving said *invasive cleavage structure*, followed by a detection of the cleavage structure, effecting the detection of the target sequence, wherein the target sequence is selected from a Markush Group.

Claim 1 of U.S. Patent No. 5,846,717, hereto referred to as '717 patent, is drawn to a method for detecting a target nucleic acid molecule by detecting non-target cleavage products, via use of oligonucleotides capable of forming an *invasive cleavage structure*, as defined on page 69 of the instant specification, and a cleavage means, followed by the detection of the non-target cleavage product, which *is* the invasive cleavage structure, thereby meeting all of the limitation of instant claim 6.

While claim 1 of the '717 patent does not explicitly state that the target nucleic acid sequence could be selected from a list of elements from the Markush group recited in instant claim 6, such limitation is considered to be obvious in view of the disclosure of Caskey et al., wherein the artisans explicitly state that, "various infectious disease can be diagnosed by the presence in clinical samples of specific DNA sequences characteristic of the causative microorganisms...includ[ing] viruses such as cytomegalovirus." (column 10, line 63 through column 11, line 13), cytomegalovirus being one of the elements recited in the Markush group of instant claim 6.

Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made, to become motivated to employ the detection method disclosed by the '717 patent for the detection of cytomegalovirus, for the purpose of detecting whether a host was infected with such infectious microorganism, with a reasonable expectation of success.

Claim 6 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,348,314 (IDS ref # 9) in view of Caskey et al (U.S. Patent No. 5,578,458, issued November 26, 1996).

Claim 6 of the instant application is drawn to a method for detecting a target sequence via use of oligonucleotides capable of forming an *invasive cleavage structure* in the target sequence and an agent capable of cleaving said *invasive cleavage structure*, followed by a detection of the cleavage structure, effecting the detection of the target sequence.

Claim 1 of U.S. Patent No. 6,348,314, hereto referred to as '314 patent, is drawn to a method for detecting a target nucleic acid molecule by detecting non-target cleavage products, via use of oligonucleotides capable of forming an *invasive cleavage structure*, as defined on page 69 of the instant specification, and a cleavage agent, followed by the detection of the non-target cleavage product, which *is* the invasive cleavage structure. Although claim 1 of '314 patent recites the nature of the target nucleic acid sequence as well as the mixture of the target nucleic acid with the oligonucleotides and the cleavage agent, such description is embraced by sub-step (b) of the instant claim 1, wherein it recites, "exposing the sample to said oligonucleotides and said agent," rendering instant claim 6 obvious in view of claim 1 of '314 patent.

While claim 1 of the '314 patent does not explicitly state that the target nucleic acid sequence could be selected from a list of elements from the Markush group recited in instant claim 6, such limitation is considered to be obvious in view of the disclosure of Caskey et al., wherein the artisans explicitly state that, "various infectious disease can be diagnosed by the presence in clinical samples of specific DNA sequences characteristic of the causative microorganisms...includ[ing] viruses such as cytomegalovirus." (column 10, line 63 through column 11, line 13), cytomegalovirus being one of the elements recited in the Markush group of instant claim 6.

Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made, to become motivated to employ the detection method disclosed by the '314 patent for the detection of cytomegalovirus, for the purpose of detecting whether a host was infected with such infectious microorganism, with a reasonable expectation of success.

Conclusion

Claims 1-3 and 5-11 are rejected.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (703) 308-9348. The Examiner can normally be reached from 8:30 a.m. to 7:00 p.m. Monday through Thursday. If attempts to reach the Examiner by telephone are unsuccessful, the Primary Examiner in charge of the prosecution, Dr. Kenneth Horlick, can be reached at (703)-308-3905. If the attempts to reach the above Examiners are unsuccessful, the Examiner's supervisor, Gary Benzion, can be reached at (703) 308-1119. Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If

applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (703) 872-9306. For Unofficial documents, faxes can be sent directly to the Examiner at (703) 746-3172. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Young J. Kim

12/1/03